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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/658,659	09/08/00	STANTON	V

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WESLEY B AMES
BROBECK PHLEGER & HARRISON LLP
12390 EL CAMINO REAL
SAN DIEGO CA 92130

EXAMINER	
CHAKRABARTI,A	
ART UNIT	**PAPER NUMBER**
1655	2

DATE MAILED: 01/10/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/658,659	Stanton
Examiner	**Group Art Unit**
Arun Chakrabarti	1655

☒ *Responsive to communication(s) filed on* Sep 8, 2000 .

☐ *This action is* **FINAL.**

☐ *Since this application is in condition for allowance except for formal matters,* **prosecution as to the merits is closed** *in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.*

A shortened statutory period for response to this action is set to expire 3 *month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).*

Disposition of Claims

☒ *Claim(s)* 1-16 *is/are pending in the application.*

Of the above, claim(s) _____ *is/are withdrawn from consideration.*

☐ *Claim(s)* _____ *is/are allowed.*

☒ *Claim(s)* 1-16 *is/are rejected.*

☐ *Claim(s)* _____ *is/are objected to.*

☐ *Claims* _____ *are subject to restriction or election requirement.*

Application Papers

☐ *See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.*

☐ *The drawing(s) filed on* _____ *is/are objected to by the Examiner.*

☐ *The proposed drawing correction, filed on* _____ *is* ☐*approved* ☐*disapproved.*

☐ *The specification is objected to by the Examiner.*

☐ *The oath or declaration is objected to by the Examiner.*

Priority under 35 U.S.C. § 119

☐ *Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).*

☐ *All* ☐ *Some** ☐ *None of the CERTIFIED copies of the priority documents have been*

☐ *received.*

☐ *received in Application No. (Series Code/Serial Number)* _____ .

☐ *received in this national stage application from the International Bureau (PCT Rule 17.2(a)).*

**Certified copies not received:* _____ .

☒ *Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).*

Attachment(s)

☒ *Notice of References Cited, PTO-892*

☐ *Information Disclosure Statement(s), PTO-1449, Paper No(s).* _____

☐ *Interview Summary, PTO-413*

☐ *Notice of Draftsperson's Patent Drawing Review, PTO-948*

☐ *Notice of Informal Patent Application, PTO-152*

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Specification

1. The attempt to incorporate essential subject matter into this application by reference to wild type gene sequences corresponding to the different mutant genes of the claims is improper because a SEQ ID Nos: of all wild type genes are required to carry out proper search of the mutant nucleic acid probe of the claimed invention.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.Attention is directed to the decision of *Vas-Cath inc. V. Mahurkar* 19 USPQ2d 1111 (CAFC, 1991):

> This court in *Wilder* (and the CCPA before it) clearly recognized, and we hereby reaffirm, that 35 USC 112, first paragraph, requires a "written description of the invention" which is separate and distinct from the enablement requirement. The

> purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the "applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed.*

Claims of the subject application have been interpreted as encompassing any allelic variant of any of the nucleic acids that encode any wild type version of the enzyme as found in any life form. At best the specification has been found to identify point mutations that have been found in but one base or wild type sequence. It is not readily apparent what the source was for each of the wild type sequences. Assuming *arguendo*, that the wild type sequences identified via a Genbak repository number, were all from a human, or constitute a consensus sequence derived from a number of humans, the specification has not been found to provide an adequate written description of other wild type versions of the coding sequence as found in other life forms, much less identify regions of variance therein and lesser still the probes encompassed by the claims of the subject application. For the above reasons, and in the absence of evidence to the contrary, the subject application has not been found to reasonably suggest that applicant was in possession of all of the probes claimed.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-4, 11 and 15 are rejected over the recitation of the word "or". Regarding claims 1-4, the word "or" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention.

Claim 7 is indefinite in absence of a period and a part of a parenthesis which started with PNA at the end rendering the claim incomplete.

Claims 10, 14 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language. These claims are an omnibus type of claims.

Claim 15 is rejected as indefinite because the instantly claimed method lacks a final process step that clearly relates back to the preamble. For the method of claim 15, the preamble of the instantly claimed method is drawn to a method for determining the presence or absence of variance in a gene while the final process step is that of contacting at least a portion of the gene or a sequence complementary thereto with a probe and it is thus unclear as to whether the instantly claimed method is drawn to method for determining the presence or absence of variance in a gene or rather contacting at least a portion of the gene or a sequence complementary thereto with a probe. Method claim requires a last step or phrase in the last step that states the accomplishments of the goals

for the method which were stated in the method's preamble. Claim 15 lacks such a last step and is confusing because the additional method step is not sufficiently set forth. While minute details are not required in method claims, at least the basic steps must be recited in a positive, active fashions. See Ex parte Erlich, 3 USPQ2d1011, p.1011 (Bd. Pat. Applicant. Int. 1986). It is suggested that an amended claim more clearly describing the intended steps be submitted.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

7. Claims 1-5, 8, 11-13 and 15 are rejected under 35 U.S.C. 102 (e) as being anticipated by Gonzalez et al. (U.S. Patent 6,015,673) (January 18, 2000).

Gonzalez et al teach an isolated, purified nucleic acid probe comprising a nucleic acid sequence 7 to 500 nucleotide bases in length that specifically binds under selective binding conditions to a nucleic acid sequence comprising at least one variance in a dihydropyrimidine dehydrogenase gene (Abstract, Claims 1 and 9, Example 4, Table 1).

Gonzalez et al teach a nucleic acid probe comprising a nucleic acid sequence less than 200, 100 or 25 nucleotide bases in length (Claim 9, Example 4, Table 1).

Gonzalez et al teach a nucleic acid probe wherein the probe comprises DNA (Abstract, Claims 1 and 9, Example 4, Table 1).

Gonzalez et al teach a nucleic acid probe wherein the probe further comprises detectable label (Example 2, Column 22, line 67 to column 23, line 5).

Gonzalez et al teach a method for determining the presence or absence of a variance in a dihydropyrimidine dehydrogenase gene, comprising contacting at least a portion of the gene or a sequence complementary thereto with a probe under selective binding conditions (Abstract, Claims 1, 4 and 9 and Examples 1, 2 and 4).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1-9, 11-13 and 15 are rejected under 35 U.S.C. 103 (a) over Gonzalez et al. (U.S. Patent 6,015,673) (January 18, 2000) in view of Billing-Medel et al. (U.S. Patent 6,130,043) (October 10, 2000).

Gonzalez et al teach probes , detectable labels and methods of claims 1-5, 8, 11-13 and 15 as described above.

Gonzalez et al do not teach probes comprising nucleic acid analogs including peptide nucleic acid.

Billing-Medel et al teach probes comprising nucleic acid analogs including peptide nucleic acid (Abstract, Column 13, lines 45-67 and Example 10).

Gonzalez et al do not teach probes comprising a fluorescent label.

Billing-Medel et al teach probes comprising a fluorescent label (Example 4, Column 44, lines 40-41, lines 58-61 and column 45, lines 16-21).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method of PNA analogs and fluorescent labels of Billing-Medel et al. in the method of Gonzalez et al., since Billing-Medel et al. state, "PNAs are neutrally charged moieties which can be directed against RNA targets or DNA. PNA probes used in assays in place of, for example, the DNA probes of the present invention, offer advantages not achievable when DNA probes are used. These advantages include manufacturability, large scale labeling, reproducibility, stability, insensitivity to changes in ionic strength and resistance to enzymatic degradation which is present in methods utilizing DNA or RNA. These PNAs can be labeled with such signal generating compounds as fluorescein, radionucleotides, chemiluminescent compounds and the like. PNAs or other nucleic acid analogs such as

Mas thus can be used in assay methods in place of DNA or RNA (Column 13, lines 51-64)". An ordinary practitioner would have been motivated to combine and substitute the method of PNA analogs and fluorescent labels of Billing-Medel et al. in the method of Gonzalez et al. in order to achieve the express advantages noted by Billing-Medel et al. of nucleic acid analogs which offer advantages include manufacturability, large scale labeling, reproducibility, stability, insensitivity to changes in ionic strength and resistance to enzymatic degradation which is present in methods utilizing DNA or RNA and which can be labeled with such signal generating compounds as fluorescein, radionucleotides, chemiluminescent compounds and the like and thus can be used in assay methods in place of DNA or RNA.

10. Claims 1-5, 8 and 10-16 are rejected under 35 U.S.C. 103 (a) over Gonzalez et al. (U.S. Patent 6,015,673) (January 18, 2000) in view of Kaneda et al. (Journal of Biological Chemistry, (1990), Vol. 265 (33), pages 20277-20284).

Gonzalez et al teach probes , detectable labels and methods of claims 1-5, 8, 11-13 and 15 as described above.

Gonzalez et al do not teach probe comprising a variance listed in Table 10.

Kaneda et al teach probes comprising a variance of Thymidylate synthase gene listed in Table 10. (Figure 2, Genbank Accession No. D00596, Page 20277)

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the TS mutant probe of

Kaneda et al. in the method of Gonzalez et al., since Kaneda et al. state, "The availability of these mutant lines and the cloned DNAs have enabled us to map the human TS gene locus to the telomeric band of chromosome 18 and also to start analyzing the mechanism of control of expression of the TS gene at both cellular and tissue levels (Page 20277, column 2, lines 32-37)". An ordinary practitioner would have been motivated to combine and substitute the cloned DNAs of Kaneda et al. in the method of Gonzalez et al. in order to achieve the express advantages noted by Kaneda et al of the availability of a nucleic acid variance which provides mapping the human TS gene locus to the telomeric band of chromosome 18 and also to analyze the mechanism of control of expression of the TS gene at both cellular and tissue levels.

Conclusion

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Arun Chakrabarti,

Patent Examiner,

January 02, 2001

B. L. Sisson

BRADLEY L. SISSON
PRIMARY EXAMINER
GROUP 1800/1655

1/8/01